IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent application of:

Applicant(s):	Hartlep et al.
Serial No:	10/661,827
Filing Date:	September 12, 2003
Title:	DETERMINING DISTRIBUTION FOR PLANNING AN INFUSION
Examiner:	Elmer M. Chao
Art Unit:	3737
Docket No.	SCHWP0177USA

SUBSTITUTE APPEAL BRIEF

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The undersigned submits this brief for the Board's consideration of the appeal of the Examiner's decision, mailed September 3, 2008, finally rejecting claims 1-16 and 18-22 of the above-identified application.

The fee for filing an appeal brief is being submitted herewith. In the event an additional fee or extension of time is necessary, the Commissioner is authorized to charge any additional fee which may be required, and further to consider this a petition for an extension of time to make the filing of this brief timely, to Deposit Account No. 18-0988 under the above-indicated docket number.

I. Real Party in Interest

The real party in interest in the present appeal is BrainLab, AG.

II. Related Appeals and Interferences

Neither appellant, appellant's legal representative, nor the prior assignee of the present application are aware of any appeals or interferences which will directly affect, which will be directly affected by, or which will have a bearing on the Board's decision in the pending appeal.

III. Status of Claims

Claims 1-16 and 18-22 are pending in the application and stand finally rejected. Claim 17 has been canceled. Claims 1-16 and 18-22 are the subject of this appeal, and a correct copy of these claims is reproduced in the Claims Appendix.

IV. Status of Amendments

No claim amendments were filed subsequent to the issuance of the final Office Action, from which this appeal is taken.

V. Summary of Claimed Subject Matter

The following is a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, which refers to the specification by page and line number in brackets, and to the drawing by reference characters.

Claim 1

1. A method for planning the introduction of a fluid in a tissue, the method comprising:

capturing via an imaging system (1) functional anatomical data and/or structural anatomical data before infusion of a fluid into the tissue [2/22-23];

evaluating the captured functional and/or structural anatomical data with computer assistance (2) and without use of an infusion fluid [2/23-25];

based on the evaluating step, identifying directional channels within the tissue and determining infusion distribution information related to the identified directional channels, the identified directional channels and/or infusion distribution information being indicative of advantageous and/or non-advantageous infusion regions [2/25-3/10]; and

presenting identified advantageous and/or non-advantageous infusion regions for viewing by a user [7/6-8]; and

based on the advantageous and/or non-advantageous infusion regions, using medical navigation to introduce an infusion device at a selected point [7/9-11].

Claim 18

18. A device for assisting planning for introducing an infusion fluid into regions of the brain, said device comprising:

an imaging device (1) that captures functional and/or structural anatomical data before an infusion of fluid into regions of the brain [5/26-29];

a processor (2) which is programmed to:

perform and assist in evaluating the functional and/or structural anatomical data in order to identify directional channels within the regions of the brain and determine infusion distribution information related to the identified directional channels, the directional channels and infusion distribution information being indicative of advantageous and non-advantageous infusion regions [6/21-27]; and

produce and evaluate a distribution simulation apart from the regions of the brain before the infusion fluid is infused, the distribution simulation being indicative of an infusion fluid when it is introduced at particular points, on the basis of the captured anatomical data [7/1-8]; and

a computer-assisted, medical planning and navigation system (3) for assisting in positioning an infusion device [7/9-21].

Claim 22

22. A method for planning the introduction of a fluid in a tissue, the method comprising:

capturing via an imaging system (1) functional anatomical data and/or structural anatomical data before infusion of any infusion fluid into the tissue [2/22-23];

evaluating the captured functional and/or structural anatomical data with computer assistance (2) [2/23-25];

based on the evaluating step, identifying directional channels within the tissue and determining infusion distribution information related to the identified directional channels, the identified directional channels and/or infusion distribution information

being indicative of advantageous and/or non-advantageous infusion regions [2/25-3/10]; and

presenting identified advantageous and/or non-advantageous infusion regions for viewing by a user [7/6-8]; and

based on the advantageous and/or non-advantageous infusion regions, using medical navigation to introduce an infusion device at a selected point [7/9-11].

VI. Grounds of Objection/Rejection to Be Reviewed on Appeal

A. Claims 1, 3-12, 21 and 22 stand rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,026,316 (referred to as *Kucharczyk*).

B. Claim 16 stands rejected under 35 U.S.C. §103(a) as being unpatentable over *Kucharczyk*.

C. Claims 2, 13-15, 18 and 19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Kucharczyk* in view of U.S. Patent No. 6,272,370 (referred to as *Gillies*).

D. Claim 20 stands rejected under 35 U.S.C. §103(a) as being unpatentable over *Kucharczyk* in view of *Gillies* in further view of U.S. Patent No. 6,233,476 (referred to as *Strommer*).

VII. Argument

The rejections advanced by the Examiner are improper and should be reversed for at least the following reasons.

Background and Summary of the Invention

Various medical methods require therapeutic agents to be directly infused into the tissue, with the aim of achieving a broad and optimum homogeneity of the distribution of the infusion fluid in the tissue to be treated. However, the homogeneity of the distribution of an infusion or of an infusion fluid can deteriorate if the infusion agent is introduced into a region in which the agent is transported through directional channels, which are not in themselves the infusion target, nor their end points. Instead of diffusing into the actual target areas, the infusion agent runs off along these "tracks", without achieving the desired effect.

The present invention provides a system and method for identifying advantageous and/or non-advantageous infusion regions in a tissue. More particularly, functional and/or structural anatomical data can be captured and the anatomical data can be evaluated with respect to the distribution information contained therein, such as directional and/or velocity information. This can be used, for example, to identify, before the infusion fluid is introduced, the directional channels at which infusion fluid may be expected to be rapidly transported away when it is introduced. The basis for this is formed by anatomical data such as can be obtained, for example, by an imaging system, such as a nuclear spin tomograph, a computer tomograph or similar known imaging systems. In this way, it is possible both to capture structural anatomical data (only data on the tissue structure) and to obtain functional information, for example, data on certain regions having a specific function (auditory cortex, visual cortex, etc.) in the brain.

Using this information along with computer assistance, the regions of the tissue that contain transport pathways can be determined. In this way, it can be determined if

the infusion agent will run off along so-called "tracks" without any effect if it is introduced at a particular point, or whether there will be a homogeneous diffusion into the surrounding tissue. Thus, before performing an infusion, it is possible to distinguish target areas having advantageous distribution properties from those having less advantageous or non-advantageous distribution properties.

The target areas having advantageous and/or non-advantageous infusion regions can be output for review, and used in conjunction with medical navigation to introduce an infusion device at a selected point.

A. Rejection of Claims 1, 3-12, 21 and 22 Under 35 U.S.C. §102(b)

Claims 1, 3-12, 21 and 22 stand rejected under 35 U.S.C. §102(b) as being anticipated by *Kucharczyk*. Reversal of the rejection is respectfully requested for at least the following reasons.

Claim 1

Claim 1 sets forth a method for planning the introduction of a fluid in a tissue, the method including, *inter alia*, capturing via an imaging system functional anatomical data and/or structural anatomical data before infusion of a fluid into the tissue, evaluating the captured functional and/or structural anatomical data with computer assistance and without use of an infusion fluid, and based on the evaluating step, ***identifying directional channels within the tissue and determining infusion distribution information related to the identified directional channels***, wherein the identified directional channels and/or infusion distribution information are indicative of

advantageous and/or non-advantageous infusion regions. Then, advantageous and/or non-advantageous infusion regions are presented for viewing by a user, and based on the identified regions, medical navigation is used to ***introduce an infusion*** *device at a selected point.*

The method according to claim 1 facilitates the identification of advantageous and/or non-advantageous infusion regions based on a capture and evaluation of functional and/or structural anatomical data ***before infusion of a fluid into the tissue***. Based on the identified advantageous and non-advantageous regions, an infusion device is introduced into the patient.

The Examiner comments in support of the rejection of claim 1 are set forth below.

> 4. **Claims 1, 3-12, 21, and 22** are rejected under 35 U.S.C. 102(b) as being anticipated by Kucharczyk et al. (U.S. 6,026,316).
>
> Regarding **claims 1, 3-5, 7, 10-12, 21, and 22,** Kucharczyk et al. teach a method for planning the introduction of a fluid in a tissue, the method comprising: capturing via an imaging system functional anatomical data and/or structural anatomical data before infusion of a fluid into the tissue (Fig. 7, second box from the top); evaluating the captured functional and/or structural anatomical data with computer assistance and without the use of an infusion fluid (Fig. 7, three horizontal boxes third from the top); based on the evaluating step, identifying directional channels within the tissue and determining infusion distribution information related to the identified directional channels, the identified directional channels and/or infusion distribution information being indicative of advantageous and/or non-advantageous infusion regions (Fig. 7, sixth box from the bottom); and presenting identified advantageous and/or non-advantageous infusion regions for viewing by a user (Fig. 7, sixth box from the bottom); and based on the advantageous and/or non-advantageous infusion regions, using medical navigation to introduce an infusion device at a selected point (Fig. 7, last box & three horizontal boxes third from the top).

In rejecting claim 1, the Examiner relies on Fig. 7 of *Kucharczyk*, which is reproduced below. More specifically, the Examiner identifies the sixth box from the bottom of Fig. 7 (referred to hereinafter as the "box 3")[1] as teaching based on the evaluating step, ***identifying directional channels within the tissue*** and determining infusion distribution information related to the identified directional channels, the identified directional channels and/or infusion distribution information being indicative of advantageous and/or non-advantageous infusion regions.

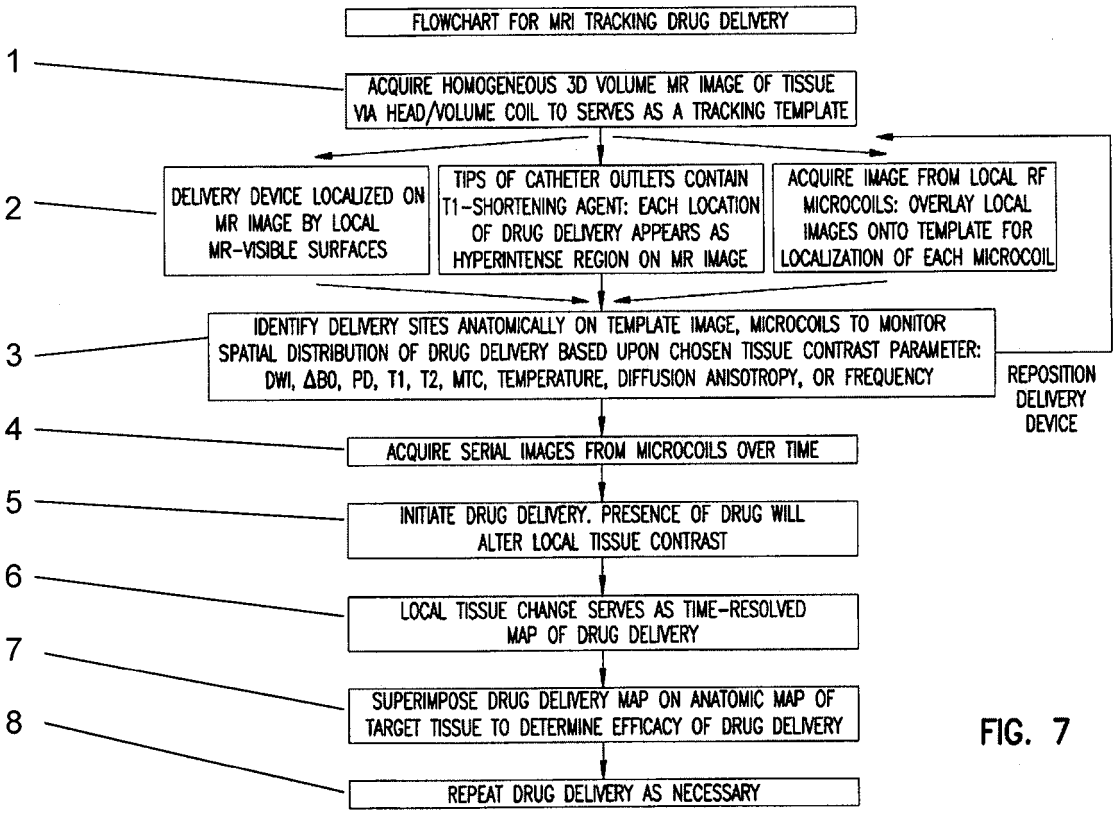

FIG. 7

Box 3 discloses that delivery sites are identified anatomically on the template image. In other words, box 3 anatomically identifies ***where*** the catheter will be inserted

[1] The boxes shown in Fig. 7 of *Kucharczyk* are identified herein as boxes 1-8, wherein box 1 is the first box after the title, box 8 is the last box, and box 2 is considered to be the three boxes in a single row. The numbers next to each box have been added for ease of understanding and are not actually shown in Fig. 7 of *Kucharczyk*

in order to deliver the agent. Identifying such delivery sites (i.e., where the catheter will be inserted), however, does not ***identify directional channels within the tissue*** as set forth in claim 1.

Additionally, box 3 discloses that microcoils are used to ***monitor the spatial distribution of the drug delivery*** based on chosen tissue contrast parameters, temperature, diffusion anisotropy, or frequency. This portion of box 3 is in preparation for actual drug delivery (e.g., for monitoring drug delivery after infusion). However, since the drug has not yet been delivered (the drug is not delivered until box 5 of Fig. 7), and since *Kucharczyk* determines efficacy of drug delivery by monitoring the distribution of the drug using MR images (see boxes 6 and 7 of Fig. 7), this portion of the box 3 also does not disclose identifying ***directional channels in the tissue*** as recited in claim 1.

In response to the above comments, the Examiner provides the following rebuttal.

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that Kucharczyk does not teach "capturing via an imaging system functional anatomical data and/or structural anatomical data before infusion of a fluid into the tissue". However, the claimed invention does not specifically state that the step of capturing can be done without the use of any infusion fluid. As Applicants have pointed out in the arguments, Kucharczyk's Fig. 7 does show that at least a second infusion is repeated after analysis of the first infusion. Therefore, Kucharczyk's teaching does satisfy the claimed limitation based on the fact that the subsequent infusion and therby injection of the infusion fluid is done after the analysis. Based on a previous interview conducted, Examiner recalls Applicants' hesistation to use the phrase "any infusion fluid" instead of the phrase "an infusion fluid". Therefore, Examiner cannot interpret the claims as they stand to convey the idea of not using "any infusion fluid". Examiner believes that the actual scope of this invention lies somewhere inbetween the literal interpretations of the phrases "any infusion fluid" and "an infusion fluid". In order to properly overcome Kucharczyk, Applicants are advised to provide antecedant basis for the phrase "infusion fluid" and/or "fluid" and correspond that phrase to the original intruduction of the fluid. Then, the steps of the subsequently claimed capturing and evaluating steps can be recited to eliminate the use of that specific infusion fluid, thereby overcoming Examiner's interpretation of Kucharczyk. Regarding the limitation "identifying direction channels within the tissue and determining infusion distribution information related to the identified channels", Examiner informs Applicants that as these limitations are worded, they can be reasonably interpreted first and foremost as mental steps. Furthermore, Applicants do not describe what it means specifically to "identify directional channels". However, Examiner has provided Applicants with Kucharczyk's explicit example of actually mapping the drug delivery (see at least fig. 7, fourth box from the bottom). Examiner asserts that this action of "mapping the drug delivery" would definitely satisfy the limitation "identify directional channels" to one of ordinary skill in the art.

The Examiner initially addresses applicant's alleged argument that *Kucharczyk* does not teach the "capturing" step of claim 1. Reviewing the record, however, applicant has not alleged that *Kucharczyk* does not teach this step. Thus, the Examiner's comments with respect to the "capturing" step of claim 1 do nothing more than cloud the issues.

The Examiner then further states that the step of identifying directional channels as set forth in claim 1 can be reasonably interpreted as a mental step. The Examiner provides no further comment regarding such mental step or why the issue was raised. Presumably, the Examiner is suggesting that the step of "identifying" is a mental step that renders the claim non-statutory. To the extent the Examiner considers claim 1 non-statutory because the "identifying" step is considered a mental step, this would amount to a new rejection that should be addressed in a new Office Action.

Moreover, it is respectfully submitted that for §101 purposes, it is irrelevant whether the "identifying" step can be considered a mental step, as other steps recited in claim 1 clearly place the claim within the requirements of §101 (e.g., capturing via an imaging system..., using medical navigation to introduce an infusion device...). Accordingly, even if the Examiner considers the "identifying" step to be a mental step, this does not render claim 1 non-statutory.

Further, the Examiner asserts Fig. 7 of *Kucharczyk* provides an explicit example of mapping the drug delivery as claimed (the Examiner points to box 5 of Fig. 7 as teaching this step). The Examiner then states that this action of "mapping the drug delivery" would definitely satisfy the limitation of "indentifying directional channels". Appellants disagree with the Examiner for at least the following reasons.

As noted above, claim 1 sets forth identifying directional channels within the tissue. Boxes 1-5 of Fig. 7 say nothing with regard to identifying directional channels and, thus, these boxes cannot reasonably be relied upon for teaching the instant feature of claim 1. However, and although not expressly stated, it is presumed that the Examiner equates boxes 6 and/or 7 as identifying directional channels in the tissue.

Assuming such interpretation, it is clear that the steps in boxes 6 and 7 are performed ***after a drug delivery device has been inserted in the patient*** (drug delivery occurs at box 5, which is prior to boxes 6 and 7). Therefore, if boxes 6 and 7 are relied upon for teaching identifying directional channels, then it follows that the infusion device used in performing the steps of Fig. 7 ***must already have been positioned and inserted into the tissue*** prior to boxes 6 and 7. If the infusion device is inserted before identifying directional channels, it follows that Fig. 7 cannot reasonably be understood to teach presenting advantageous and/or non-advantageous infusion regions for viewing, and then ***based on the identified infusion regions*** using medical navigation to ***introduce an infusion device*** as claimed.

Regarding the Examiner's comment in the Advisory Action that *Kucharczyk* shows a second infusion is repeated, it is noted that *Kucharczyk* expressly provides that ***drug delivery is repeated as necessary*** (box 8). "Drug delivery" in Fig. 7 of *Kucharczyk* begins at box 5 and, thus, only boxes 5-8 are understood to be repeated, none of which include introducing the delivery device. In other words, the steps related to "repeating drug delivery" are understood to retain the same delivery site, without moving the delivery device. Accordingly, boxes 5-8 (i.e., the repeated boxes) are not understood to disclose ***based on the advantageous and non-advantageous infusion regions, using medical navigation to introduce an infusion device***.

Claim 6

Claim 6 depends from claim 1 and thus the above comments with respect to claim 6 are also applicable to claim 1. Claim 6 further recites, *inter alia*, making

adjustments in the distribution information, the adjustments being responsive to anatomical or structural conditions which have changed over a period of time. The Examiner's comments in support of the rejection of claim 6 are set forth below.

> Regarding **claim 6**, Kucharczyk et al. teach evaluating the functional and/or structural anatomical data over a period of time with respect to the distribution information (Fig. 7, third box from the top); and making adjustments in the distribution information, said adjustments being responsive to anatomical or structural conditions which have changed over the period of time (Fig. 7, last four boxes).

Box 3 of Fig. 7 discloses that delivery sites are identified anatomically on a template image, and that microcoils are used to monitor the spatial distribution of a drug delivery based on various parameters. In the context of Fig. 7, the microcoils are used to monitor the spatial distribution of the drug delivery after the drug has actually been delivered. This delivery does not occur until a later step (i.e., box 5), and thus box 3 cannot reasonably be interpreted as disclosing that functional and/or structural anatomical data are evaluated over a period of time with respect to the ***distribution information***.

Regarding making adjustments as set forth in claim 6, the Examiner relies on boxes 5-8 of Fig. 7. Summarizing these boxes, the drug delivery is initiated (box 5), the local tissue changes as a result of the delivery (box 6), a map of the drug delivery is superimposed on an anatomic map of the target tissue to determine efficacy of drug delivery (box 7) and the drug delivery is repeated (box 8). Nowhere in boxes 5-8 is there any reference to making adjustments in the distribution information as set forth in claim 6.

Accordingly, a *prima facie* case of obviousness has not been established for claim 6.

Claim 21

Claim 21 depends from claim 1 and thus the above comments with respect to claim 1 are also applicable to claim 21. Claim 21 further recites obtaining diffusion measurements before infusion via magnetic resonance diffusion imaging and indentifying transport pathways based on the diffusion measurements.

In the final Office Action, the Examiner, other than stating claim 21 is anticipated by *Kucharczyk*, does not provide any specific comment with regard to the rejection of claim 21. However, in the Office Action dated September 4, 2007, the Examiner does comment on the rejection of claim 21, and these comments are set forth below.

> Regarding **claims 1, 16, and 21,** Kucharczyk '316 discloses a method for identifying advantageous and non-advantageous infusion regions in a tissue (Fig 7, 4th box down), said method comprising: capturing via an imaging system structural anatomical data before infusion of a fluid into the tissue (Fig 7); evaluating the captured structural anatomical data with computer assistance (the methods of Fig 7 inherently require computer assistance); and based on the evaluating step, identifying direction channels within the tissue and determining infusion distribution information related to the identified directional channels, the identified direction channels and/or infusion distribution information being indicative of advantageous and/or non-advantageous infusion regions; presenting identified advantageous and/or non-advantageous infusion regions for viewing by a user; and identifying transport pathways based on the diffusion measurements (Fig 7, 4th and 5th boxes down, the MRI images would identify all of the diffusion details).

In rejecting claim 21, the Examiner alleges that boxes 4 and 5 disclose identifying transport pathways based on diffusion measurements. Appellants respectfully disagree.

Box 4 of Fig. 7 discloses that serial images are obtained over time, and box 5 discloses that drug delivery is initiated. Nowhere in these boxes, however, is there any reference to identifying transport pathways, let alone identifying such pathways based on magnetic resonance diffusion imaging. Regarding any steps performed subsequent to the steps in box 5, these steps occur after drug delivery has been initiated and thus are not "before infusion" as claimed. Accordingly, *Kucharczyk* has not been shown to teach all the features of claim 21.

B. Rejection of claim 16 under 35 U.S.C. §103(a)

Claim 16 depends from claim 1 and thus can be distinguished from *Kucharczyk* for at least the same reasons set forth in Section A above.

C. Rejection of Claims 2, 13-15, 18 and 19 Under 35 U.S.C. §103(a)

Claim 2

Claim 2 depends from claim 1 and thus the above comments with respect to claim 1 are also applicable to claim 2. Claim 2 further sets forth that evaluating the captured functional and/or structural anatomical data includes simulating apart from the tissue a distribution of an infusion at a plurality of regions in the tissue. The Examiner's comments in support of the rejection of claim 2 are set forth below.

Regarding **claim 2**, Kucharczyk et al. teach the limitations as discussed above but failed to explicitly teach the evaluating step including simulating the infusion at a plurality of regions in the tissue. However, in the same field of endeavor Gillies et al. teach simulating the infusion at a plurality of regions in the tissue (col. 16, line 28 - col. 17, line 21). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to simulate the infusion at a plurality of regions in the tissue in order to predict the response of the tissue to infusion before actually carrying out the infusion procedure (for motivation see col. 16, line 32-34).

The cited portion of *Gillies* is reproduced below.

Basser has developed a biophysical model for infusions through a porous medium like the brain ("Interstitial Pressure, Volume, and Flow during Infusion into Brain Tissue," Microvascular Research, Vol. 44, pps. 143-165, 1992). In particular, he uses a consolidation model to predict the dynamic response of the brain's structure to the pressure-driven infusion of a fluid within the brain. He then examines the pressure and flow distributions for infuisates pumped into the brain under four different conditions. (1) infusion from a constant pressure source, (2) infusion from a constant flow source, (3) step infusion from a pressure source, and (4) step infusion from a constant flow source. infusion from a constant pressure source is a model that is applicable to the delivery of drugs into the bulk brain tissues, and one of the results of Basser's study is the prediction that the velocity, $V_r(r)$, of the fluid infused within the brain is a function of the radial distance, r, from the infusion point, and that the specific prediction is that $V_r(r)=kP_o\ a/r^2\ f$ where k is the hydraulic conductivity of the brain matrix material, P_o is the pressure within the cavity created in the brain matrix at the tip of the infusion source (eg., the catheter tip) by the initial influx of fluid, a is the radius of the initial infusion cavity, and f is the volume fraction of the interstitial space relative to the total brain volume. The penetrability of fluids agents delivered via pressure-driven infusion is generally different from that associated strictly with diffusion of the same substances, since the driving mechanisms are different (infusion: flow along a pressure gradient; diffusion: flow along a concentration gradient). This is an important point since diffusion alone may not constitute a completely effective driving mechanism for all of the different fluid agents that must penetrate certain regions of the brain e.g., those with elevated interstitial pressure, such as solid tumors (for a discussion of elevated intersitial pressure in tumors, see Netti et al., "Time-Dependent Behavior of Interstitial Fluid Pressure in Solid Tumors: Implications for Drug Delivery," Cancer Research, Vol. 55, pps. 5451-5458, 1995). Moreover, Morrison et al. ("High-Flow Microinfusion: Tissue

> Penetration and Pharmacodynamics," American Journal of Physiology, Vol. 266, ps. R292-R305, 1994) have shown that volumetric infusion rates of 0.5µl/min and above are potentially able to provide dosages of agents to much larger volumes of brain tissues than are possible with lower-flow rate methods. These points, taken in conjunction with clinical testing of the infusion concept (Lieberman et al., "Convection-Enhanced Distribution of Large Molecules in Gray Matter During Interstitial Drug Infusion, Journal of Neurosurgery, Vol. 82, pps. 1021-1029, 1995; Laske et al., "Chronic Interstitial Infusion of Protein to Primate Brain: Determination of Drug Distribution and Clearance with Single-Photon Emission Computerized Tomography Inaging, Journal of Neurosurgery, Vol.87, pps. 586-594, 1997; Broaddus et al., "distribution and Stability of Antisense Phosphorothioate Oligonucleotides in Rodent Brain Following Direct Intra parenchymal Controlled-Rate bIfusion," Neurosurgical Focus, Vol. 3, No. 5, Article 4, 1997), suggests the utility of the method for treating a wide variety for neurological disorders, providing that a suitable means of placing the catheter within the brain and verifying its proper location therein can be employed. The present invention provides appropriate methodology for allowing this to happen.

The Examiner admits that *Kucharczyk* does not disclose simulating a distribution of an infusion at a ***plurality of regions in the tissue***, but contends this feature is disclosed in *Gillies*. Appellants respectfully disagree.

The cited portion of *Gillies* discloses a biophysical model for infusion through a porous medium, such as the brain. More particularly, a consolidation model is disclosed for predicting the dynamic response of the brain's structure to pressure driven infusion of a fluid within the brain. However, no discussion is found with respect to simulating a distribution of an infusion at a ***plurality of regions in the tissue***, as set forth in claim 2. Thus, the Examiner has shown all the features in the cited art and, therefore, has not established a *prima facie* case of obviousness with respect to claim 2.

Claim 18

Claim 18 sets forth a device for assisting planning for introducing an infusion fluid into regions of the brain, the device including, *inter alia*, a processor programmed to perform and assist in evaluating the functional and/or structural anatomical data in order to ***identify directional channels*** with the regions of the brain. The Examiner's comments in support of the rejection of claim 18 are set forth below.

> Regarding **claims 13-15, 18, and 19**, Kucharczyk et al. teach all of the above limitations. Kucharczyk et al. does not explicitly teach the infusion at the selected point being planned using stereotactic planning and navigation. However, Gillies et al. teach the use of stereotactics in combination with magnetic resonance imaging in the planning and navigation for drug delivery (abstract). Therefore, it would have been obvious to a person of ordinary skill in the art at the time of the invention to modify Kucharczyk et al. to use Gillies et al.'s method to perform the infusion after the infusion site has been selected. Such a modification would produce a method of drug delivery that is more accurate and less damaging to other areas around the target area (col. 10, lines 1-9).

Since the Examiner only addresses one issue in claim 18, it is presumed the Examiner takes the position that all the other features of claim 18 are disclosed in *Kucharczyk*. As discussed above with respect to claim 1, *Kucharczyk* is not understood to teach identifying directional channels as claimed. More particularly, box 3 of Fig. 7 (which the Examiner has relied on for teaching identifying directional channels[2]) discloses that delivery sites are identified anatomically on the template image. In other words, box 3 anatomically identifies *where* the catheter will be inserted in order to deliver the agent. Identifying such delivery sites (i.e., where the catheter will be placed),

[2] See page 3, top of the final Office Action

however, does not ***identify directional channels within regions of the brain***, as set forth in claim 18.

Regarding the microcoils referenced in box 3, they are used during actual delivery of the drug (i.e., at box 5). Since the drug has not yet been delivered at box 3, and since *Kucharczyk* determines efficacy of drug delivery by monitoring the actual distribution of the drug using MR images (see boxes 6 and 7 of Fig. 7), this portion of box 3 also does not disclose identifying *directional channels within regions of the brain* as recited in claim 18.

Regarding *Gillies*, the Examiner does not indicate where in *Gillies* the above features are disclosed. Accordingly, the Examiner has not shown that *Kucharczyk* in view of *Gillies* discloses all the features of claim 18 and, thus has not established a *prima facie* case of obviousness.

D. Rejection of Claim 20 Under 35 U.S.C. §103(a)

Claim 20 depends from claim 18 and thus the above comments with respect to claim 18 are applicable to claim 20. Further, *Gillies* and *Strommer* have not been found to make up for the deficiencies of *Kucharczyk* and, thus, claim 18 is distinguishable from *Kucharczyk* in view of *Gillies* and *Strommer*. Since claim 20 depends from claim 18, claim 20 is also distinguishable from *Kucharczyk* in view of *Gillies* and *Strommer*.

VIII. Conclusion

In view of the foregoing, it is respectfully submitted that the claims are patentable over the applied art and that the rejections advanced by the Examiner should be reversed.

Respectfully submitted,

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Claims Appendix

1. A method for planning the introduction of a fluid in a tissue, the method comprising:

capturing via an imaging system functional anatomical data and/or structural anatomical data before infusion of a fluid into the tissue;

evaluating the captured functional and/or structural anatomical data with computer assistance and without use of an infusion fluid;

based on the evaluating step, identifying directional channels within the tissue and determining infusion distribution information related to the identified directional channels, the identified directional channels and/or infusion distribution information being indicative of advantageous and/or non-advantageous infusion regions; and

presenting identified advantageous and/or non-advantageous infusion regions for viewing by a user; and

based on the advantageous and/or non-advantageous infusion regions, using medical navigation to introduce an infusion device at a selected point.

2. The method as set forth in claim 1, wherein evaluating the captured functional and/or structural anatomical data includes simulating apart from the tissue a distribution of an infusion at a plurality of regions in the tissue.

3. The method as set forth in claim 1, wherein the determined infusion distribution information includes direction information and/or velocity information relating to infusion regions in the tissue.

4. The method as set forth in claim 1, wherein the functional and/or structural anatomical data is evaluated two-dimensionally with respect to the distribution information which it contains.

5. The method as set forth in claim 1, wherein the functional and/or structural anatomical data is evaluated three-dimensionally with respect to the distribution information which it contains.

6. The method as set forth in claim 1, further comprising:

evaluating the functional and/or structural anatomical data over a period of time with respect to the distribution information; and

making adjustments in the distribution information, said adjustments being responsive to anatomical or structural conditions which have changed over the period of time.

7. The method as set forth in claim 3, further comprising:

identifying regions of rapid diffusion.

8. The method as set forth in claim 3, further comprising:

determining isotropy and anisotropy of flow directions in the regions in the tissue.

9. The method as set forth in claim 1, further comprising:

calculating a distribution volume for an infusion fluid from the functional and/or structural anatomical data.

10. The method as set forth in claim 1, wherein the functional and/or structural anatomical data is captured two-dimensionally.

11. The method as set forth in claim 10, wherein a number of two-dimensional data sets on the functional and/or structural anatomical data are combined to obtain three-dimensional information.

12. The method as set forth in claim 1, wherein the functional and/or structural anatomical data is captured three-dimensionally.

13. A method for assisting planning for introducing an infusion fluid into regions of a brain, said method comprising:

identifying infusion regions using a method as set forth in claim 1; and

wherein introducing the infusion at a selected point is planned using stereotactic planning.

14. A method for assisting navigation for introducing an infusion into regions of a brain, said method comprising:

identifying the infusion regions and positions for an infusion device are identified using a method as set forth in claim 1; and

wherein introducing the infusion device at a selected point is planned using stereotactic navigation.

15. The method as set forth in claim 13, wherein anatomical, functional and/or structural tissue data are combined with information on a distribution of the infusion fluid to be expected for planning or navigation.

16. A computer-readable medium storing a computer program, wherein when the program is loaded onto a computer and executed, the program causes the computer to carry out the steps as set forth in claim 1.

18. A device for assisting planning for introducing an infusion fluid into regions of the brain, said device comprising:

an imaging device that captures functional and/or structural anatomical data before an infusion of fluid into regions of the brain;

a processor which is programmed to:

perform and assist in evaluating the functional and/or structural anatomical data in order to identify directional channels within the regions of the brain and determine infusion distribution information related to the identified directional channels, the directional channels and infusion distribution information being indicative of advantageous and non-advantageous infusion regions; and

produce and evaluate a distribution simulation apart from the regions of the brain before the infusion fluid is infused, the distribution simulation being indicative of an infusion fluid when it is introduced at particular points, on the basis of the captured anatomical data; and

a computer-assisted, medical planning and navigation system for assisting in positioning an infusion device.

19. The device as set forth in claim 18, wherein the imaging device includes a nuclear spin tomograph.

20. The device as set forth in claim 18, wherein the imaging device, the processor and the medical planning and navigation system are connected to each other via data connections, thereby providing a constant or retrievable exchange of data.

21. The method as set forth in claim 1, further comprising obtaining diffusion measurements before infusion via magnetic resonance diffusion imaging and identifying transport pathways based on the diffusion measurements.

22. A method for planning the introduction of a fluid in a tissue, the method comprising:

capturing via an imaging system functional anatomical data and/or structural anatomical data before infusion of any infusion fluid into the tissue;

evaluating the captured functional and/or structural anatomical data with computer assistance;

based on the evaluating step, identifying directional channels within the tissue and determining infusion distribution information related to the identified directional channels, the identified directional channels and/or infusion distribution information being indicative of advantageous and/or non-advantageous infusion regions; and

presenting identified advantageous and/or non-advantageous infusion regions for viewing by a user; and

based on the advantageous and/or non-advantageous infusion regions, using medical navigation to introduce an infusion device at a selected point.

Evidence Appendix

None.

Related Proceedings Appendix

None.